



RAW SEQUENCE LISTING ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 09/643,128
Source: 600
Date Processed by STIC: 11/21/03

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.

PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
- 2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY

FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 703-308-4212; FAX: 703-308-4221

Effective 12/13/03: TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE **CHECKER VERSION 4.1 PROGRAM**, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

<http://www.uspto.gov/web/offices/pac/checker/chkr41note.htm>

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.

Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.

Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<<http://www.uspto.gov/ebc/efs/downloads/documents.htm>> , EFS Submission User Manual - ePAVE)
2. U.S. Postal Service: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. Hand Carry directly to (EFFECTIVE 12/01/03):
U.S. Patent and Trademark Office, Box Sequence, Customer Window, Lobby, Room 1B03, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202
4. Federal Express, United Parcel Service, or other delivery service to: U.S. Patent and Trademark Office, Box Sequence, Room 4B03-Mailroom, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202

Revised 10/08/03

Raw Sequence Listing Error Summary

ERROR DETECTED	SUGGESTED CORRECTION	SERIAL NUMBER: <u>09/643,128</u>
ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE		
1. <u> </u> Wrapped Nucleics Wrapped Aminos	The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping."	
2. <u> </u> Invalid Line Length	The rules require that a line not exceed 72 characters in length. This includes white spaces.	
3. <u> </u> Misaligned Amino Numbering	The numbering under each 5 th amino acid is misaligned. Do not use tab codes between numbers; use space characters , instead.	
4. <u> </u> Non-ASCII	The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text.	
5. <u> </u> Variable Length	Sequence(s) <u> </u> contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.	
6. <u> </u> PatentIn 2.0 "bug"	A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s) <u> </u> . Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.	
7. <u> </u> Skipped Sequences (OLD RULES)	Sequence(s) <u> </u> missing. If intentional, please insert the following lines for each skipped sequence: (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) (i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading) (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) This sequence is intentionally skipped Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.	
8. <u> </u> Skipped Sequences (NEW RULES)	Sequence(s) <u> </u> missing. If intentional, please insert the following lines for each skipped sequence. <210> sequence id number <400> sequence id number 000	
9. <u> </u> Use of n's or Xaa's (NEW RULES)	Use of n's and/or Xaa's have been detected in the Sequence Listing. Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present. In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.	
10. <u> </u> Invalid <213> Response	Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence	
11. <u> </u> Use of <220>	Sequence(s) <u> </u> missing the <220> "Feature" and associated numeric identifiers and responses. Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section. (See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules)	
12. <u> </u> PatentIn 2.0 "bug"	Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.	
13. <u> </u> Misuse of n/Xaa	"n" can only represent a single nucleotide; "Xaa" can only represent a single amino acid	



IFW16

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/643,128

DATE: 11/21/2003

TIME: 11:01:32

Input Set : A:\PTO.YF.txt

Output Set: N:\CRF4\11212003\I643128.raw

4 <110> APPLICANT: Jifan Hu, GMR Epigenetics Corporation;
 5 Andrew R. Hoffman, Stanford University
 7 <120> TITLE OF INVENTION: Gene Inactivation by Targeted DNA Methylation
 9 <130> FILE REFERENCE: 10853-005-999
 C--> 11 <140> CURRENT APPLICATION NUMBER: US/09/643,128
 12 <141> CURRENT FILING DATE: 2000-08-21
 14 <150> PRIOR APPLICATION NUMBER: US60/96,749
 15 <151> PRIOR FILING DATE: 2000-04-12
 17 <160> NUMBER OF SEQ ID NOS: 56
 19 <170> SOFTWARE: PatentIn For Windows v. 3

Global error.
Consult Sequence Rules.
Consult sample Sequence Listing
(attached)
pp 1-5

ERRORED SEQUENCES

21 <210> SEQ ID NO: 1
 22 <211> LENGTH: 5
 23 <212> TYPE: DNA
 24 <213> ORGANISM: Artificial sequence
 W--> 26 <220> FEATURE: Hairpin *this belongs on 22237 line*
 W--> 27 <221> NAME/KEY: m5C
 28 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-methylcytidine (m5C) at CpG
 29 dinucleotide sequence
 31 <400> SEQUENCE: 1
 E--> 32 m5cgtm5cg *delete "m5" - show nucleotide only*
 36 <210> SEQ ID NO: 2
 37 <211> LENGTH: 5
 38 <212> TYPE: DNA
 39 <213> ORGANISM: Artificial sequence
 W--> 41 <220> FEATURE: Hairpin *Same error*
 W--> 42 <221> NAME/KEY: m5C
 43 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-methylcytidine (m5C) at CpG
 44 dinucleotide sequence
 46 <400> SEQUENCE: 2
 E--> 47 m5cgtm5cg *"n" needs explanation in 22207-22237 section. (see item 9 on Error summary sheet)*
 51 <210> SEQ ID NO: 3
 52 <211> LENGTH: 10
 53 <212> TYPE: DNA
 54 <213> ORGANISM: Artificial sequence
 W--> 56 <220> FEATURE: Hairpin
 W--> 57 <221> NAME/KEY: m5C
 58 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-methylcytidine (m5C) at CpG

59 dinucleotide sequence
61 <400> SEQUENCE: 3

RAW SEQUENCE LISTING

DATE: 11/21/2003

PATENT APPLICATION: US/09/643,128

TIME: 11:01:32

Input Set : A:\PTO.YF.txt

Output Set: N:\CRF4\11212003\I643128.raw

do not show dashes

E--> 62 cgacg~~tm5cgtm5cg~~
66 <210> SEQ ID NO: 4
67 <211> LENGTH: 22
68 <212> TYPE: DNA
69 <213> ORGANISM: Artificial sequence

W--> 71 <220> FEATURE: Hairpin

W--> 72 <221> NAME/KEY: m5C

73 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-methylcytidine (m5C) at CpG

74 dinucleotide sequence

76 <300> PUBLICATION INFORMATION:

77 <301> AUTHORS: Xiaoming Yao, Ji-Fan Hu, Mark Daniels, Hadas Shiran, Xiangjun Zhou, Huifan

78 Yan,
79 Hongqi Lu, Zhilan Zeng, Qingxue Wang, Tao Li, and Andrew R. Hoffman

80 <302> TITLE: A methylated oligonucleotide inhibits IGF2 expression and enhances survival in a model of hepatocellular carcinoma

82 in a model of hepatocellular carcinoma

83 <303> JOURNAL: Journal of Clinical Investigation

W--> 84 <307> DATE: in press

86 <400> SEQUENCE: 4

E--> 87 agccm5cgggm5ctgggaggagtm5cgg
91 <210> SEQ ID NO: 5
92 <211> LENGTH: 33
93 <212> TYPE: DNA
94 <213> ORGANISM: Artificial sequence

W--> 96 <220> FEATURE: Hairpin

W--> 97 <221> NAME/KEY: m5C

98 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-methylcytidine (m5C) at CpG

99 dinucleotide sequence

101 <300> PUBLICATION INFORMATION:

102 <301> AUTHORS: Xiaoming Yao, Ji-Fan Hu, Mark Daniels, Hadas Shiran, Xiangjun Zhou, Huifan

103 Yan,
104 Hongqi Lu, Zhilan Zeng, Qingxue Wang, Tao Li, and Andrew R. Hoffman

105 <302> TITLE: A methylated oligonucleotide inhibits IGF2 expression and enhances survival in a model of hepatocellular carcinoma

107 in a model of hepatocellular carcinoma

108 <303> JOURNAL: Journal of Clinical Investigation

W--> 109 <307> DATE: in press

111 <400> SEQUENCE: 5

E--> 112 cgacg~~tm5cgtm5cg~~agccm5cgggm5ctgggaggagtm5cgg
116 <210> SEQ ID NO: 6
117 <211> LENGTH: 22
118 <212> TYPE: DNA
119 <213> ORGANISM: Artificial sequence

121 <220> FEATURE:

W--> 122 <221> NAME/KEY:

123 <223> OTHER INFORMATION: Phosphothioate oligonucleotide

125 <300> PUBLICATION INFORMATION:

126 <301> AUTHORS: Xiaoming Yao, Ji-Fan Hu, Mark Daniels, Hadas Shiran, Xiangjun Zhou, Huifan

127 Yan,

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/643,128

DATE: 11/21/2003

TIME: 11:01:32

Input Set : A:\PTO.YF.txt

Output Set: N:\CRF4\11212003\I643128.raw

128 Hongqi Lu, Zhilan Zeng, Qingxue Wang, Tao Li, and Andrew R. Hoffman
 129 <302> TITLE: A methylated oligonucleotide inhibits IGF2 expression and enhances
 130 survival
 131 in a model of hepatocellular carcinoma
 132 <303> JOURNAL: Journal of Clinical Investigation

W--> 133 <307> DATE: in press

135 <400> SEQUENCE: 6

E--> 136 ggtcacgggtcaggcgtatggtg

140 <210> SEQ ID NO: 7

141 <211> LENGTH: 21

142 <212> TYPE: DNA

143 <213> ORGANISM: Artificial sequence, c-myc

W--> 145 <220> FEATURE: Hairpin

W--> 146 <221> NAME/KEY: m5C

147 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-
 methylcytidine (m5C) at CpG

148 dinucleotide sequence

150 <400> SEQUENCE: 7

E--> 151 tm5cgctaatctcm5cgcccaom5cgg

154 <210> SEQ ID NO: 8

155 <211> LENGTH: 20

156 <212> TYPE: DNA

157 <213> ORGANISM: Artificial sequence, c-myc

W--> 159 <220> FEATURE: Hairpin

W--> 160 <221> NAME/KEY: m5C

161 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-
 methylcytidine (m5C) at CpG

162 dinucleotide sequence

164 <400> SEQUENCE: 8

E--> 165 acm5cggccctttataatcm5cga

169 <210> SEQ ID NO: 9

170 <211> LENGTH: 20

171 <212> TYPE: DNA

172 <213> ORGANISM: Artificial sequence, c-myc

W--> 174 <220> FEATURE: Hairpin

W--> 175 <221> NAME/KEY: m5C

176 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-
 methylcytidine (m5C) at CpG

177 dinucleotide sequence

179 <400> SEQUENCE: 9

E--> 180 tm5cgcccaom5cggccctttat

184 <210> SEQ ID NO: 10

185 <211> LENGTH: 18

186 <212> TYPE: DNA

187 <213> ORGANISM: Artificial sequence, HIV

W--> 189 <220> FEATURE: Hairpin

W--> 190 <221> NAME/KEY: m5C

191 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-
 methylcytidine (m5C) at CpG

192 dinucleotide sequence

194 <400> SEQUENCE: 10

E--> 195 cam5cgtagcm5cgagacm5ctg

199 <210> SEQ ID NO: 11

group into 10's

22 ← insert

this goes on <2237> line.

Do not insert explanation on

<2137

line.

group into 10's

21 ←

c-myc

group into 10's

20 ←

c-myc

10's

20 ←

c-myc

10's

18 ←

FYI
 The sequence is throughout
 the sequence and contains
 several errors

IMPORTANT

<110> Smith, John: Smithgene Inc.

<120> Example of a Sequence Listing

<130> 01-00001

<140> PCT/EP98/00001
<141> 1998-12-31

<150> US 08/999,999
<151> 1997-10-15

<160>

<170> PatentIn version 2.0

<210> 1
<211> 389
<212> DNA
<213> Paramecium sp.

<220>
<221> CDS
<222> (279)...(389)

<300>
<301> Doe, Richard
<302> Isolation and Characterization of a Gene Encoding a
Protease from Paramecium sp
<303> Journal of Genes
<304> 1
<305> 4
<306> 1-7
<307> 1988-06-31
<308> 123456
<309> 1988-06-31

<400>	1						60
agctgtagtc	attcctgtgt	ccctctctct	ctgggcttct	cacctctcta	atcagatctc		
agggagagtg	ctctgacctt	ccctctgctt	tgacagcttca	caggcaggca	ggcaggcagc		120
tgatctggca	attgctggca	gtgccacagg	ctctttagcc	aggctttagg	tggttccgpr		180
cgcggcgccg	cggccctctt	cgcgctctct	tcgcgctctt	ctctctgctt	ccctctgctc		240

Consult

Appendix 3, page 2

```

ggacctgall aggtgagcag gaggagggggg cagtttagc 290
Met Val Ser Met Phe Ser
1 5

ttg tct ttc aaa tgg cct gga tct tgt ttg btt gtt tgt ttg ttc caa 344
Leu Ser Phe Lys Trp Pro Gly Phe Cys Leu Phe Val Cys Leu Phe Gln
10 15 20

tgt ccc aaa gtc ctc ccc tgt cac tca tca ctg cag ccg aat ctt 389
Cys Pro Lys Val Leu Pro Cys His Ser Ser Leu Gln Pro Asn Leu
25 30 35

<210> 2
<211> 37
<212> PRT
<213> Paramecium sp.

<<00> 2
Met Val Ser Met Phe Ser Leu Ser Phe Lys Trp Pro Gly Phe Cys Leu
1 5 10 15

Phe Val Cys Leu Phe Gln Cys Pro Lys Val Leu Pro Cys His Ser Ser
20 25 30

Leu Gln Pro Asn Leu
35

<210> 3
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> Designed peptide based on size and polarity to act as a
linker between the alpha and beta chains of Protein XYZ.

<400> 3
Met Val Asn Leu Glu Pro Met His Thr Glu Ile
1 5 10

<210> 4
<400> 4
000

```

[Annex VIII follows]

identifiers and their accompanying information as shown in the following table. The numeric identifier shall be used only in the "Sequence Listing." The order and presentation of the items of information in the "Sequence Listing" shall conform to the arrangement given below. Each item of information shall begin on a new line and shall begin with the numeric identifier enclosed in angle brackets as shown. The submission of those items of information designated with an "M" is mandatory. The submission of those items of information designated with an "O" is optional. Numeric identifiers <110> through <170> shall only be set forth at the beginning of the "Sequence Listing." The following table illustrates the numeric identifiers.

Numeric Identifier	Definition	Comments and Format	Mandatory (M) or Optional (O)
<110>	Applicant	Preferably max. of 10 names; one name per line; preferable format: Surname, Other Names and/or Initials	M
<120>	Title of Invention		M
<130>	File Reference	Personal file reference	M, when filed prior to assignment of appl. number
<140>	Current Application Number	Specify as: US 07/999,999 or PCT/US96/99999	M, if available
<141>	Current Filing Date	Specify as: yyyy-mm-dd	M, if available
<150>	Prior Application Number	Specify as: US 07/999,999 or PCT/US96/99999	M, if applicable include priority documents under 35 USC 119 and 120
<151>	Prior Application Filing Date	Specify as: yyyy-mm-dd	M, if applicable
<160>	Number of SEQ ID NOs	Count includes total number of SEQ ID NOs	M
<170>	Software	Name of software used to create the Sequence Listing	O
<210>	SEQ ID NO:M:	Response shall be an integer representing the SEQ ID NO shown	M
<211>	Length	Respond with an integer expressing the number of bases or amino acid residues	M

<212>	Type	<p>Whether presented sequence molecule is DNA, RNA, or PRT (protein). If a nucleotide sequence contains both DNA and RNA fragments, the type shall be "DNA." In addition, the combined DNA/RNA molecule shall be further described in the <220> to <223> feature section.</p>	M
<213>	Organism	<p>Scientific name, i.e. Genus/species, Unknown or Artificial Sequence. In addition, the "Unknown" or "Artificial Sequence" organisms shall be further described in the <220> to <223> feature section.</p>	M
<220>	Feature	<p>Leave blank after <220>. <221-223> provide for a description of points of biological significance in the sequence.</p>	<p>M, under the following conditions: if "n," "Xaa," or a modified or unusual L-amino acid or modified base was used in a sequence; if ORGANISM is "Artificial Sequence" or "Unknown" the molecule is combined DNA/RNA.</p>
<221>	Name/Key	<p>Provide appropriate identifier for feature, preferably from WIPO Standard ST. 25 (1998), Appendix 2, Tables 5 and 6</p>	<p>M, under the following conditions: if "n," "Xaa," or a modified or unusual L-amino acid or modified base was used in a sequence</p>
<222>	Location	<p>Specify location within sequence; where appropriate state number of first and last bases/amino acids</p>	<p>M, under the following conditions: if "n," "Xaa," or a modified or unusual L-amino acid or modified</p>

		in feature	base was used in a sequence
<223>	Other Information	Other relevant information; four lines maximum	H, under the following conditions: if "n," "Xaa," or a modified or unusual L-amino acid or modified base was used in a sequence; if ORGANISM is "Artificial Sequence" or "Unknown"; if molecule is combined DNA/RNA.
<300>	Publication Information	Leave blank after <300>	0
<301>	Authors	Preferably max. of ten named authors of publication; specify one name per line; preferable format: Surname, Other Names and/or Initials	0
<302>	Title		0
<303>	Journal		0
<304>	Volume		0
<305>	Issue		0
<306>	Pages		0
<307>	Date	Journal date on which data published; specify as yyyy-mm-dd, 1001-yyyy or Season-yyyy	0
<308>	Database Accession Number	Accession number assigned by database including database name	0
<309>	Database Entry Date	Date of entry in database; specify as yyyy-mm-dd or 1001-yyyy	0
<310>	Patent Document Number	Document number; for patent-type citations only. Specify as, for example, US 07/999,999	0

<311>	Patent Filing Date	Document filing date, for patent-type citations only; specify as yyyy-mm-dd	0
<312>	Publication Date	Document publication date, for patent-type citations only; specify as yyyy-mm-dd	0
<313>	Relevant Residues	FROM (position) TO (position)	0
<400>	Sequence	SEQ ID NO should follow the numeric identifier and should appear on the line preceding the actual sequence	0

5. Section 1.024 is revised to read as follows:

1.024 Form and format for nucleotide and/or amino acid sequence submissions in computer readable form.

(a) The computer readable form required by 1.021(c) shall meet the following specifications:

(1) The computer readable form shall contain a single "Sequence Listing" as either a diskette, series of diskettes, or other permissible media outlined in paragraph (c) of this section.

(2) The "Sequence Listing" in paragraph (a) (1) of this section shall be submitted in American Standard Code for Information Interchange (ASCII) text. No other formats shall be allowed.

(3) The computer readable form may be created by any means, such as word processors, nucleotide/amino acid sequence editors or other custom computer programs; however, it shall conform to all specifications detailed in this section.

(4) File compression is acceptable when using diskette media, so long as the compressed file is in a self-extracting format that will decompress on one of the systems described in paragraph (b) of this section.

(5) Page numbering shall not appear within the computer readable form version of the "Sequence Listing" file.

(6) All computer-readable forms shall have a label permanently affixed thereto on which has been hand-printed or typed: the name of the applicant, the title of the invention, the date on which the data were recorded on the computer readable form, the operating system used, a reference number, and an application serial number and filing date, if known.

(b) Computer readable form submissions must meet these format requirements:

(1) Computer: IBM PC/XT/AT, or compatibles, or Apple Macintosh;

(2) Operating System: MS-DOS, Unix or Macintosh;